Diffusion-weighted MRI of the prostate in patients with a significant family history of prostate cancer: do histogram metrics correlate with risk?

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Target Audience: Radiologists, radiographers, physicists and clinicians with interest in Diffusion Weighted (DW) MRI of the prostate

Purpose: Risk of prostate cancer in first-degree relatives is twice that of the general population. Fifty-three single nucleotide polymorphisms (SNPs) have been shown to be significantly associated with clinically significant prostate cancers in young (<60 yr) patients with prostate cancer or those with a positive family history (1). DW-MRI has improved the sensitivity and specificity of detection of prostate cancer in the peripheral zone because tumors are recognised as regions of diffusion restriction against the background diffusivity of this highly glandular zone (2). The relationship between diffusivity and genetic risk however, has not been investigated. The purpose of this study was to evaluate whether a relationship exists between diffusion characteristics derived from histogram analysis and genetic risk.

Methods: 51 patients with a positive family history of prostate cancer, defined as (a) 1 first degree relative with histologically or death-certificate proven prostate cancer diagnosed at <70 years, (b) 2 relatives on the same side of the family, where at least one is diagnosed at <70 years, or (c) 3 relatives on the same side of the family, diagnosed at any age were recruited. Patients were excluded if they were not between 40 and 69 years in age, had suffered a previous cancer with a terminal prognosis of less than five years, had previously been diagnosed with prostate cancer or had a negative biopsy within one year. Risk scores were based on 24 SNP analysis. Images were acquired at 3T using an endorectal technique, filling the balloon with 60 ml of perfluorocarbon. T2W images in 3 planes orthogonal to the prostate (FSE 13, TR 2500ms, TE 110ms, FOV 14 cm, slice thickness 2.2 mm, matrix 220x184, extrapolated to 256x256) were complemented by DW images in the transverse plane (single shot EPI, TR 5243ms, TE 72ms, FOV 180 cm, slice thickness 2.2 mm, matrix 80x71, extrapolated to 128x128). An experienced observer drew regions of interest around the whole prostate on every slice of the ADC maps and around the central gland (CG) only with direct visual reference to the T2W image taking into account the geometric distortion of the DW images. The difference between these ROIs represented the peripheral zone (PZ). Histograms were generated with a bin width of 20 X 10^{-6}. Centile values of ADC x 10^{-6} (10^{th}, 25^{th}, 50^{th}, 75^{th} and 90^{th} centiles) derived from individual patients' histograms as well as histogram skew and kurtosis were recorded separately for the PZ and CG.

Results: Risk scores from SNP analyses were available in 40 patients and ranged from 0.29 to 4.89 (mean 1.3 $\pm$ 1.01, median 0.96). Mean values for each histogram parameter of ADC are given in ***Table 1***. Correlation coefficients between histogram derived parameters and risk score from 24 SNPs are given in ***Table 2***. There was no statistically significant correlation between histogram derived ADC parameters and risk score.

Table 1: ADC Histogram Parameters from different prostate regions

	Peripheral zone	Central gland
Centile	**Mean $\pm$ SD**	**Mean $\pm$ SD**
C10 X 10^{-6}	1083.2 $\pm$ 154.5	997.6 $\pm$ 106.4
C25 X 10^{-6}	1281.1 $\pm$ 184.9	128.5 $\pm$ 109.1
C50 X 10^{-6}	1488.2 $\pm$ 216.3	1280.0 $\pm$ 116.3
C75 X 10^{-6}	1716.5 $\pm$ 218.2	1443.8 $\pm$ 124.4
C90 X 10^{-6}	1953.9 $\pm$ 215.8	1608.1 $\pm$ 134.4
skew	0.15 $\pm$ 0.46	0.41 $\pm$ 0.30
kurtosis	3.99 $\pm$ 0.64	4.17 $\pm$ 0.98

Table 2: Correlation of histogram parametrics with Risk Scores

	Peripheral zone		Central Gland	
Centile	*Pearson (correlation coefficient)*	*P = sign*	*Pearson (correlation coefficient)*	*P = sign*
C10	-0.002	0.99	-0.01	0.93
C25	-0.01	0.95	-0.004	0.98
C50	-0.19	0.90	-0.01	0.96
C75	-0.06	0.70	-0.04	0.79
C90	-0.11	0.48	-0.05	0.73
Skew	-0.12	0.39	-0.16	0.26
Kurtosis	-0.04	0.78	0.09	0.54

Discussion and Conclusions: The derivation of risk score as <1 in 22 of 40 patients (55%) with a positive family history was unexpected. The SNPs selected may therefore be poorly indicative of risk. A further study extending the genetic analysis to all 73 SNPs known to be associated with the risk of prostate cancer is planned. Although there is currently no apparent correlation between ADC parameters and risk, further work is needed to establish whether they provide complementary information in identifying patients with clinically relevant prostate cancers.

References: (1) Goh et al, 2012, *J Intern Med*, 271, 353-365; (2) Morgan et al, 2007, *Acta Radiologica*, 48, 695-703
Acknowledgements: CRUK and EPSRC Cancer Imaging Centre in association with the MRC and Department of Health (England) grant C1060/A10334, also NHS funding to the NIHR Biomedical Research Centre